

AUG 05 2002
PATENT & TRADEMARK OFFICE

A. PE

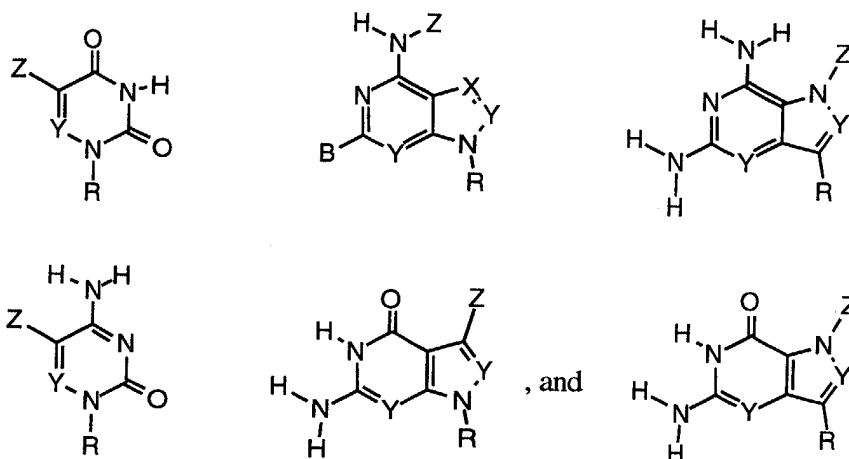
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A "clean" version of the amendment.

D1

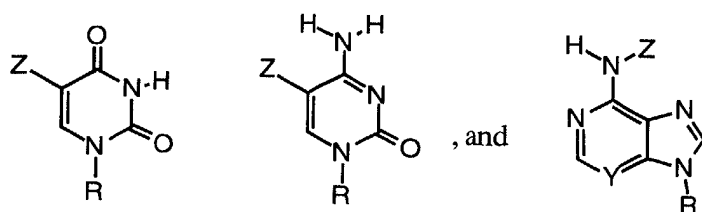
Claim 3 (amended). An improvement in a method for creating a ligand for a target compound, said method comprising:

- synthesizing a mixture of oligonucleotides from nucleotide building blocks each of the oligonucleotides having a region of randomized sequence,
- contacting said mixture with the target, wherein oligonucleotides having an increased affinity to the target relative to others in the mixture may be partitioned from the remainder of the mixture,
- partitioning the oligonucleotides with increased affinity from the other oligonucleotides in the mixture,
- amplifying the oligonucleotides having increased affinity *in vitro* to yield a mixture of oligonucleotides enriched in those with increased affinity for said target, wherein the improvement comprises including among said nucleotide building blocks those carrying nucleobases selected from the group consisting of



wherein -R designates the point of attachment to the ribose or 2'-deoxyribose ring, B is selected from the group consisting of -H or -NH₂, X is either a nitrogen atom or a carbon atom bearing a substituent Z, Z is an unfunctionalized lower alkyl, alkynyl, or alkyl-alkynyl chain, or a lower alkyl, alkynyl, or alkyl-alkynyl chain bearing an amino, carboxyl, hydroxy, thiol, aryl, indole, or imidazolyl group, Y is either N or CH, and the ring contains no more than three nitrogens consecutively bonded.

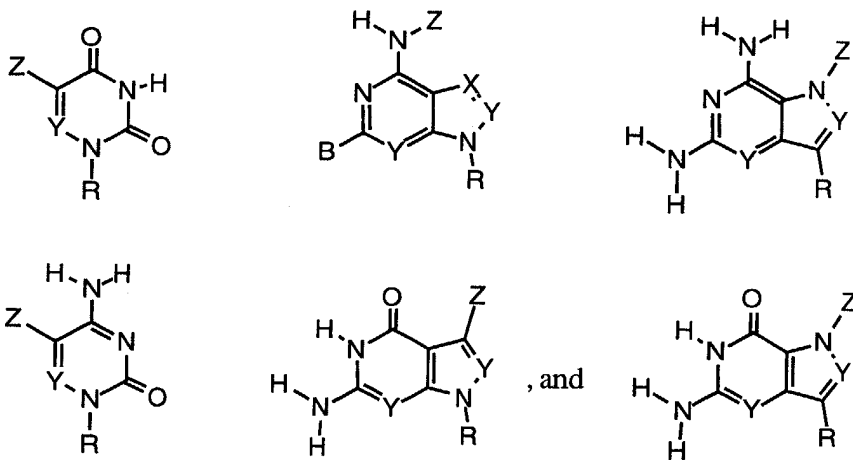
Claim 4 (amended). The improvement of Claim 3 wherein said nucleobase is selected from the group consisting of



wherein -R designates the point of attachment to the ribose or 2'-deoxyribose ring, and wherein Z is selected from the group consisting of -C=C-CH₂-NH₂, -C=C-CH₂-SH, -CH₂CH₂CH₂-NH₂, -CH₂CH₂CH₂-SH, -CH₂-NH₂, -CH₂-SH-, CH₂CH₂-NH₂, -CH₂CH₂-SH, -CH₂CH₂CH₂-imidazole, -CH₂CH₂-imidazole, lower alkyl, -CH₂-imidazole, and -CH₂CH₂CH₂CH₂CH₂-NH₂.

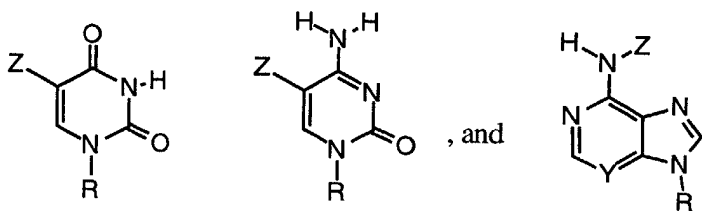
D2
Claim 7 (amended). An improvement in a method for creating a catalyst for a preselected reaction, said method comprising:

- synthesizing a mixture of oligonucleotides from nucleotide building blocks each having a region of randomized sequence
 - incubating said mixture under conditions where oligonucleotides that catalyze said reaction undergo as a result of their catalytic activity a chemical transformation that makes them preferentially separable from other oligonucleotides in the mixture having less catalytic activity,
 - separating the oligonucleotides with increased catalytic activity from the other oligonucleotides in the mixture
 - copying the oligonucleotides having increased catalytic activity *in vitro* to yield a mixture of oligonucleotides enriched in those with increased catalytic activity,
- wherein the improvement comprises including among said nucleotide building blocks those carrying nucleobases selected from the group consisting of



wherein -R designates the point of attachment to the ribose or 2'-deoxyribose ring, B is selected from the group consisting of -H or -NH₂, X is either a nitrogen atom or a carbon atom bearing a substituent Z, Z is an unfunctionalized lower alkyl, alkynyl, or alkyl-alkynyl chain, or a lower alkyl, alkynyl, or alkyl-alkynyl chain bearing an amino, carboxyl, hydroxy, thiol, aryl, indole, or imidazolyl group, Y is either N or CH, and the ring contains no more than three nitrogens consecutively bonded.

Claim 8 (amended). The improvement of Claim 7, wherein said nucleobase is selected from the group consisting of



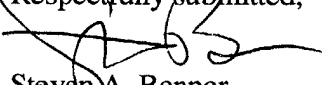
wherein -R designates the point of attachment to the ribose or 2'-deoxyribose ring, and wherein Z is selected from the group consisting of -C=C-CH₂-NH₂, -C=C-CH₂-SH, -CH₂CH₂CH₂-NH₂, -CH₂CH₂CH₂-SH, -CH₂-NH₂, -CH₂-SH-, CH₂CH₂-NH₂, -CH₂CH₂-SH, -CH₂CH₂CH₂-imidazole, -CH₂CH₂-imidazole, lower alkyl, -CH₂-imidazole, and -CH₂CH₂CH₂CH₂CH₂-NH₂.

Claim 9 (amended). An improvement in a method for creating a catalyst for a preselected reaction, said method comprising:

- synthesizing a mixture of oligonucleotides from nucleotide building blocks each having a region of randomized sequence

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- b) incubating said mixture under conditions where oligonucleotides that catalyze said reaction undergo as a result of their catalytic activity a chemical transformation that makes them preferentially separable from other oligonucleotides in the mixture having less catalytic activity ,
 - c) separating the oligonucleotides with increased catalytic activity from the other oligonucleotides in the mixture
 - d) copying the oligonucleotides having increased catalytic activity *in vitro* to yield a mixture of oligonucleotides enriched in those with increased catalytic activity, wherein said improvement comprises:
 - e) including an organic cofactor during step (b), wherein said organic cofactor binds noncovalently to the oligonucleotides and carries functionality not present on natural oligonucleotides.

Respectfully submitted,


Steven A. Benner
(Applicant)
Tel (352) 332 2262, (352) 392 7773
Fax (352) 331 0462
Email sbenner@bellsouth.net